# Cortical Control of Neural Prostheses

Final Report

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# Work Performed During the Contract Period

Under the support of this contract, we have assessed several designs for chronically implanted electrode arrays in monkeys, studied three algorithms for deriving a control signal from the ensemble activation of a sample of motor cortical neurons, written programs that allow us on-line control of a robotic arm, and created a simulated environment that allows us to test our movement extraction algorithms and control schemes.

Shortly prior to the end of this contract, we put the pieces together. We used one of our extraction algorithms to generate real-time online control of a Zebra Zero robotic arm from the activity of fewer than 30 sensorimotor cortical neurons. The online system was able to mirror a monkey's target-directed arm movements during performance of a 3d center->out reaching task.

**Electrode development and testing**

We have implanted electrodes in both hemispheres of eight rhesus monkeys. A total of 57 electrode arrays have been implanted: 3 Michigan electrodes, one self-contained microdrive designed on site, and 53 microwire arrays. Forty-six of these electrode arrays were purchased commercially (NB Labs, Dennison, TX), and the remaining 7 were made in our laboratories. About half of those arrays recorded cellular activity on at least one channel of the array during the duration of the implant. For those arrays that recorded unit activity, an average of about 9 neurons per array were recorded in the daily sessions.

Early in the contract period, we experienced some difficulty with our chronic recording techniques in the monkey preparation. The lifetime of implants was short, and the number of neurons isolated was low. In order to better understand the possible failure modes of our

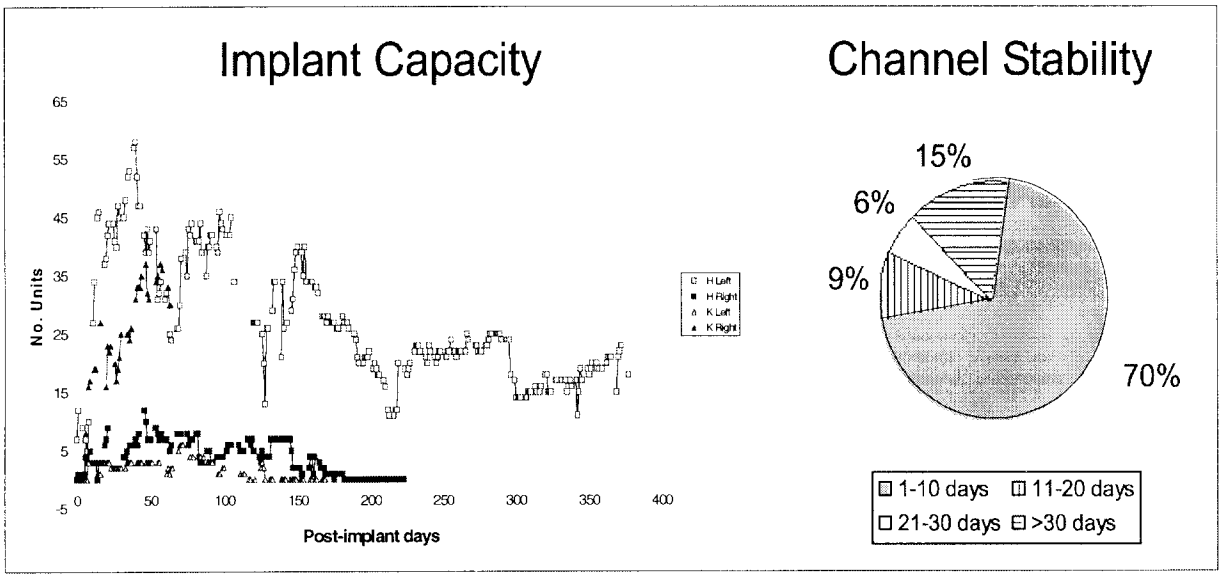


**Figure 1** *Implant capacity and stability.* On the left is shown the number of units recorded from each of four hemispheres as a function of time since the implant. Each hemisphere illustrated had a total of 64 microwires implanted. The left hemisphere on monkey H was our most successful implant to date. The right hemisphere on the same monkey is the first microdrive. The pie chart on the right breaks down the number of consecutive days of activity that were recorded on any given single channel

methods, we undertook a parallel effort to assess the microwire-based implant technique in experiments using rodents and cats. These experiments convinced us that one crucial aspect of these surgeries is the length of time the cortex is exposed. We refined our surgical techniques to decrease the amount of cortex we need to expose, and to limit the time over which it remains exposed. We also refined the electrode array design and incorporated those changes into the implants we used in the monkeys.

Figure 1 shows the effective recording periods that we obtained in four sets of implants. To the left is shown the number of cells recorded from each implant over the duration of the recording. The pie chart on the right shows a breakdown of number of consecutive days that any channel was active. Most of the channels in our implants record neurons only transiently, but 21% of the channels that became active recorded continuous activity for more than 20 days.

One of our most successful implants was a set of 4 NB electrodes that were implanted in the left hemisphere of animal H on 9/9/98. We continue to record from those implants, and currently have about 15 neurons. We believe that the remarkable stability of recording in these implants is due largely to protection of the cortex both during and after the implantation.

We have found that separate implants record activity with strikingly different physiological properties. We believe there are two possible explanations for this. First, the physiology we observe might be related to the depths of the implants, so that the properties of neuronal activity with respect to movement changes across the layers of cortex. Alternatively, independent evidence suggests that the motor cortex is not homogeneous. Function might be localized to different portions of the primary motor cortex, in which case the precise location of implants with respect to the surface of the cortex could be important.

To pursue these issues, we have developed an implantable microdrive. One advantage of our initial microdrive was that we were able to implant the microdrive, and then seal the cortex before driving the electrodes. Therefore the surface of the cortex was exposed for a shorter time, and we drove the electrodes over the space of days rather than hours. We implanted the first microdrive in monkey H on 1/13/99 (H-right in Figure 1). We recorded neurons from this implant for 113 days, until the microdrive failed. Throughout that time, recording conditions were remarkably clear and stable. Based on our experiences with the first microdrive, we have now designed and engineered a second microdrive (Figure 2). The new device is designed to drive electrodes through the dura, so that we can implant it without ever exposing the cortex. The microdrive itself consists of 12 delrin wedges mounted inside a 16 mm cylinder. Each wedge is configured with eight holes through which we can run eight 50 micron wires. The

wires are glued to the wedge with a small amount of cyanoacrylic glue, giving us bundles of 8 microwires per wedge. Each bundle can be independently lowered using screws on the outside of the microdrive.

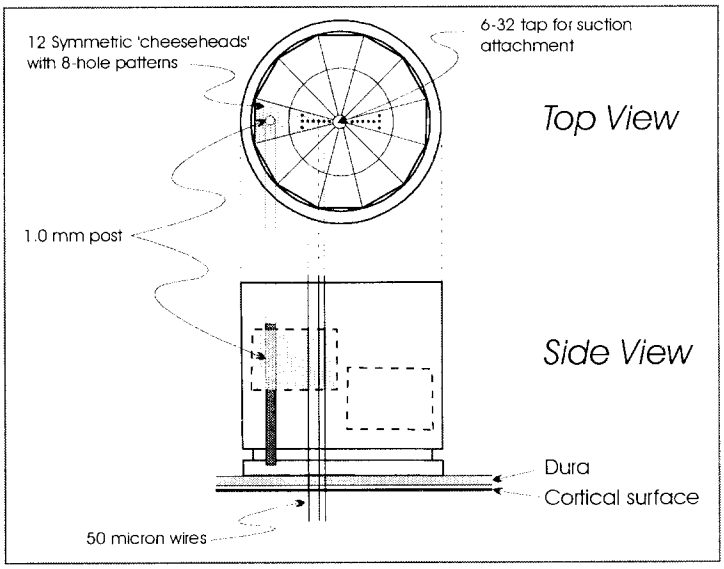


**Figure 2** *Top and side views of implantable microdrive.* The drive consists of a 16 mm chamber containing 16 Delrin wedges. Each wedge can be independently controlled to drive eight microwires through the dura and into the cortex

The top of the microdrive is fitted with a tap for the connection of a vacuum line. We believe that by applying a light vacuum to the inside of the chamber, we can hold the dura securely against the base of the microdrive. With the vacuum applied, we will drive the microwires slowly through the dura. Once through the dura, each bundle will be driven to a depth which provides optimal recording conditions. "Optimal conditions" means well-isolated single units recorded on as many channels as possible.

In its current configuration, this device has 64 microwires arranged into 8 separately controlled bundles. The spacing on this array is tight, so that we can target a large proportion of the microwires into a very small area of motor cortex.

**Data Analysis**

As detailed in our progress reports, we have also made large strides in the analysis of our data. We have developed and performed preliminary tests on three possible schemes for converting signals from a limited number of neurons to generate a control signal. One of these schemes is based on a population vector analysis. The other two are classification schemes, one

based on fuzzy logic and one based on a principal components analysis of the ensemble activation.

The population vector analysis and the principal component based scheme have shown the greatest promise thus far. In the population vector technique, each neuron contributes independently to the output control signal based on it's mean firing rate over a 20 msec time window. We have been able to generate online control signals that result in 3d movements terminating in the correct spatial octant. However, the technique is severely hampered by the small numbers of neurons that we are generally able to record thus far. The accuracy of control signals is further decreased by non-uniformity in the distribution of preferred directions.

The principal component analysis has shown greater promise in simulation. In contrast to the population vector algorithm, this method makes use of a 200 msec window of activation across the whole ensemble. Not only does each neuron provide information about movement direction in its firing pattern over a 200 msec window, but the correlations between neurons over that window also contribute to the output.

The two steps involved in this analysis are illustrated in Figs. 3 and 4. We start with multiple time windows across all the cells (Fig. 3, upper left), and concatenate them columnwise into a matrix. The first column of the matrix contains the first 200 msec of activity of all neurons broken into 20 msec bins, thus each column has NR = (number of neurons) * (10 = number of bins) entries (Fig. 3, right). Each succeeding column contains the activation for successive windows, and is associated with a movement velocity which we measured at the end of that interval.

We then construct a covariance matrix from the rows of the data matrix (Fig. 3, bottom), and extract from 9 to 30 eigenvectors from the covariance matrix. When the original data matrix is multiplied by the eigenvectors (Fig. 4), it produces a reduced ensemble activation function. Instead of NR values for each time bin, the ensemble activation function has only as many values as the number of eigenvectors used from the covariance matrix. Each time bin of the ensemble activation function retains the connection to movement velocities established in the data matrix

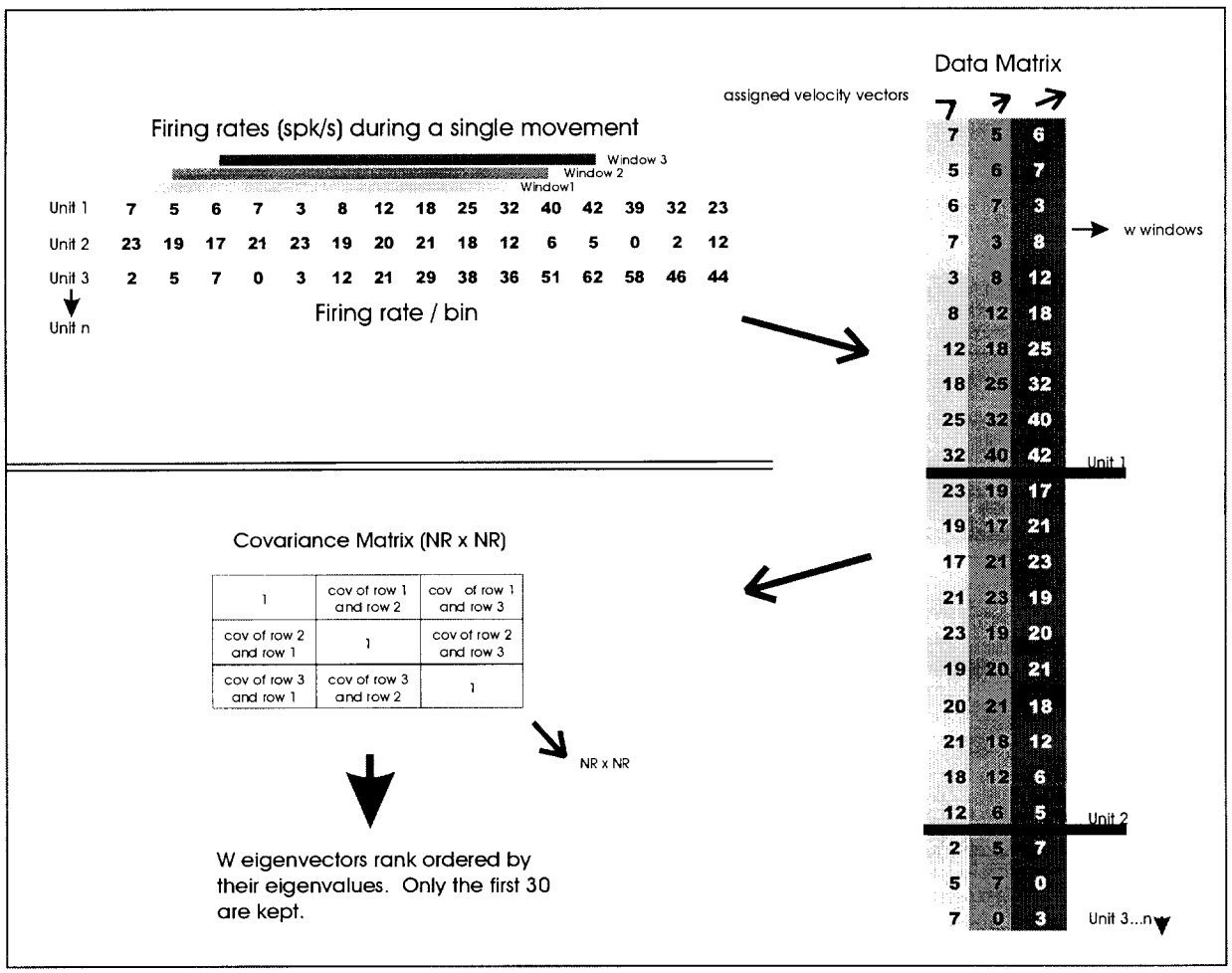


**Figure 3**. *Initial principal component analysis of ensemble data.* Data from all the neurons are binned into 20 msec bins. A 200 msec window of activation is taken from all of the neurons (top) and concatenated to form the columns of a data matrix (right). Each successive column of the data matrix contains data from a successive window, and is associated with a particular velocity of movement. A covariance matrix is constructed from the data matrix (bottom left), and the eigenvectors computed for the covariance matrix. These eigenvectors are then used to construct a reduced representation of the data contained in the data matrix.

(small arrows at the upper right of Fig. 3).

To generate a control signal from real-time ensemble activity, we start by taking a 200 msec window of activation from all of the neurons in the ensemble. All of these windows are concatenated into a single column of data (Fig. 4, left). We then multiply this column of data by each of the eigenvectors from the covariance matrix (Fig. 4, center), producing the ensemble activation at the current time window containing from 9 to 30 values (corresponding to the

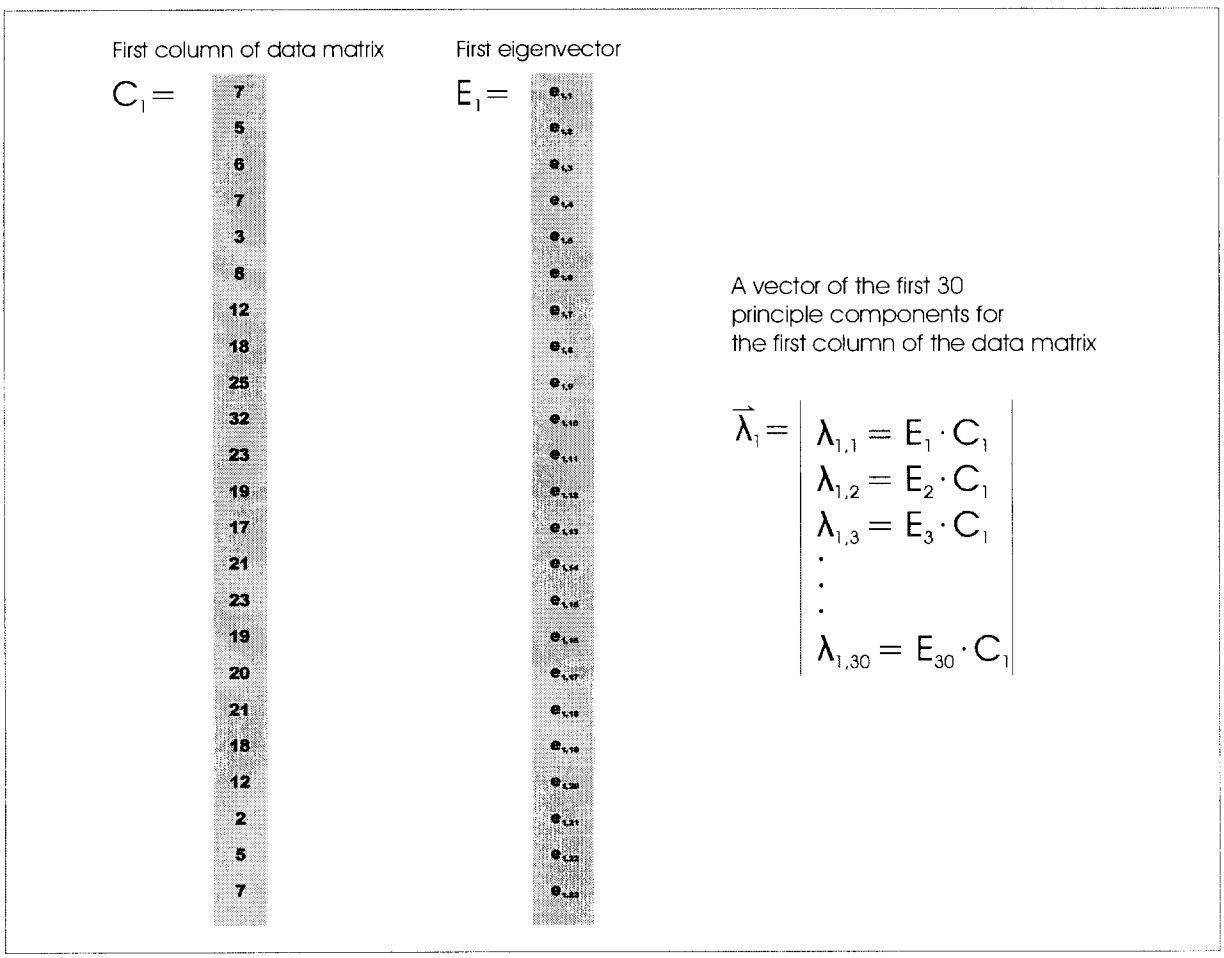


**Figure 4** *Computation of reduced ensemble activation function.* Each column of the data matrix is multiplied by the set of eigenvectors from the covariance matrix. This produces a reduced representation of the ensemble activity, $\lambda_i$, for each column 'i' of the data matrix. The same computation on real-time data produces an ensemble activation function, $\lambda_0$, which represents ongoing activity. This function, $\lambda_0$, is compared to the complete set of $\lambda_i$ to find the $\lambda_i$ which comes closest to matching $\lambda_0$.

number of eigenvectors we use, Fig. 4, right). We then compare this ensemble activation function to each column of the ensemble activation functions established previously, and find the column from that set which is most similar to the ensemble activation function at the current time. Finally, we attach the velocity vector corresponding to that column from the set to the ongoing movement.

In simulation, this scheme produces movements that not only end in the correct octant, but also follow the entire path of the hand movement with up to 80% accuracy. We have implemented an online controller that uses this method, and are currently testing and refining that controller.

**Online Control of the Robot**

We have developed software that allows us to control the Zebra Zero robotic arm in real time. This software has two components. On the data-collection side of the system is a program which takes neural data, converts it to control signals for the robot, and outputs that signal across a serial port.

On the robot side, we have software which accepts those control packets at any time interval, and interpolates across those intervals to produce velocity steps for the robot once every 7 msec.

We have been able to control the robot using purely cortical signals, as well as control signals derived from two artificial sources. First, we incorporated an artificial output into our analysis program, so that in the event the reconstruction from the data is inadequate, the program will add in the components of an idealized trajectory. Using this output we have been able to

control the robot arm as animals perform the center->out task, mimicking the monkey's target directed movements.

We have also developed a "Cyber-monkey." This is a program that generates both the behavioral events that correspond to the behaviors in our task, and spike trains from several modeled neurons that generate spikes with a Poisson distribution regulated by a cosine tuning function.

**Final Status**

Finally, we have generated real-time online control of the robotic arm in three dimensions using the population vector algorithm. We have tested the controller using input from 26 directionally-tuned neurons. This number is too low for fine control of the robot. Seventy-eight percent of the movements we have generated go towards the correct spatial quadrant, but only 29% go towards the correct octant using the PVA algorithm. We have also tested the generalizability of our control by presenting a monkey with a treat and having it reach outside the workspace defined by the eight targets. In a few cases the robot has followed the monkey's arm as the monkey reached for the treat.

We have written a program that will use the principal component based algorithm to control arm movement. Offline simulations with this technique have shown that it is capable of turning on control around the time that the monkeys actually begin movements, and following trajectories with up to 80% accuracy.

**Initial contract objectives and future research directions**

The original stated objectives in this contract were to develop

1. a reliable electrode interface for recording large numbers of units in motor cortex,
2. a control algorithm that can be implemented in real-time, and
3. the training of an animal to operate a robot arm using this control signal.

With respect to the electrode interface, our best implant has produced active recordings for well over a year. Contrasting this implant with earlier implants has led us to develop a system which we believe will provide a very stable environment for recording. This device has been constructed, and should be implanted within weeks of this report.

We have developed several algorithms to control the robotic arm, and have run two of them on-line and in real-time. We will continue refining these controllers.

We have not yet begun training an animal to make use of the control system. We plan to begin this training early in the year 2000. We will be following two tracks. In one track, we will be using a virtual-reality based system. Here the animal will see a 3D "virtual arm" moving in the place of his actual arm. This virtual arm can be controlled either in parallel with his actual arm movements, or directly from cortical activity. We will use this system to assess the animal's ability to finely control aspects of cell firing across the ensemble. For example, we will see if the animal can regulate the preferred direction of individual neurons, or the dynamic range of movement-related neurons. The purpose is to determine the extent to which an animal can adapt the firing in individual neurons to contain more information about intended movement.

In the second track, an animal will be presented directly with a robotic arm under control of the animal's ensemble cortical activation. We plan to use standard operant conditioning techniques to train the animal to control the robot using cortical signals.

## Publications under contract support

*Published and submitted manuscripts*

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*Abstracts*

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Weber DJ, RE Isaacs, J He, and AB Schwartz (1999) Response and adaptation of simultaneously recorded cortical neurons to transient perturbations in arm trajectory, *Society for Neuroscience*, Miami Beach, FL.

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